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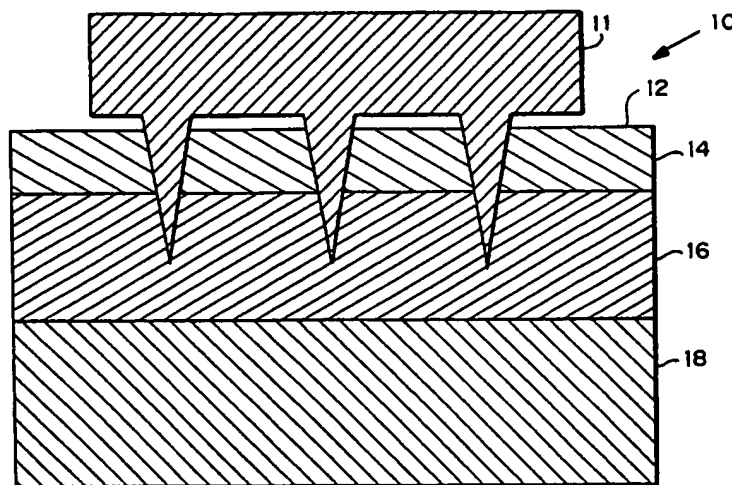
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[Continued on next page]

(54) Title: DEVICES AND METHODS FOR ENHANCED MICRONEEDLE PENETRATION OF BIOLOGICAL BARRIERS



(57) Abstract: Microneedle devices are provided for delivery of drugs across biological tissue and for controlled sampling of biological fluids in a minimally-invasive, painless, and convenient manner. The devices permit 1) drug delivery at clinically relevant rates across or into skin or other tissue barriers, and/or 2) in vivo sensing or withdrawal of biological fluids from the body, particularly from or through the skin or other tissue barriers. Drug delivery devices preferably include a plurality of hollow microneedles attached to or integrated into a substrate, and at least one reservoir (containing drug) selectively in communication with the microneedles, wherein the amount of drug to be delivered can be selectively altered. Withdrawal or sensing microneedle devices preferably include microneedles attached to or integrated into a substrate, and at least one collection chamber and/or sensor in communication with the microneedles.



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# INTERNATIONAL SEARCH REPORT

International Application No  
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A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61M37/00 A61B10/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61M A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 964 482 A (GERSTEL MARTIN S ET AL) 22 June 1976 (1976-06-22)	1-5, 9-12, 22, 23, 29-32, 41, 50-52
A	the whole document	40, 55, 60, 77, 120
X	EP 0 497 620 A (UNIV CARNEGIE MELLON) 5 August 1992 (1992-08-05)	1-4, 13, 23, 40, 41, 52
A	column 5, line 43 - line 56; figures	55, 60, 77, 120
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

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PCT/US 00/15312

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 195 25 607 A (BOEHRINGER INGELHEIM KG) 16 January 1997 (1997-01-16)	1-7, 13, 23, 40, 41, 55, 58
A	column 3, line 30 -column 5, line 30; figures	60, 62, 65, 77, 120
X	WO 98 28037 A (ALZA CORP) 2 July 1998 (1998-07-02)	40, 120
A	the whole document	1-3, 6, 41-66, 77
X	WO 98 00193 A (EPPSTEIN JONATHAN A ;SPECTRX INC (US); ALTEA TECHNOLOGIES INC (US)) 8 January 1998 (1998-01-08)	40, 77, 78, 87, 89, 96, 110, 118, 119, 121
A	abstract; figures	1, 41, 55-66
P, X	WO 99 64580 A (GEORGIA TECH RES INST) 16 December 1999 (1999-12-16)	1-36, 40-66
A	the whole document	77, 120
A	US 5 865 786 A (ROSEN SANFORD ET AL) 2 February 1999 (1999-02-02) column 12, line 53 -column 13, line 10; figures	55-66
X	WO 98 00194 A (SONTRA MEDICAL L P) 8 January 1998 (1998-01-08)	40, 55-66, 77, 78, 89, 96, 110, 121
	page 18, line 11 -page 21, line 24; figures	

# INTERNATIONAL SEARCH REPORT

international application No.  
PCT/US 00/15312

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 37-39, 67-76  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-36,41-54

A device for transport of material across or into a biological barrier comprising a plurality of hollow microneedles, a substrate to which the microneedles are attached, a reservoir in connection with at least one of the microneedles, wherein the volume or amount of material to be transported can selectively be altered.

2. Claim : 40

A kit for delivering a therapeutic fluid comprising a plurality of hollow microneedles, a substrate to which the microneedles are attached a reservoir in communication with the microneedles and a triggering device to activate delivery of the agent from reservoir through the microneedles.

3. Claims: 55-66

A device for sensing an analyte in a biological fluid, comprising a plurality of microneedles, a substrate to which the microneedles are attached and at least a sensor in communication with the microneedles.

4. Claims: 77-121

A device for transport of material across a biological barrier comprising a microneedle, a substrate to which the microneedle is attached and means for improving penetration of the biological barrier by the microneedle.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/15312

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3964482 A	22-06-1976	NONE	
EP 0497620 A	05-08-1992	US 5312456 A AT 169090 T DE 69226384 D DE 69226384 T JP 6323310 A US 5569272 A US 5676850 A	17-05-1994 15-08-1998 03-09-1998 17-12-1998 25-11-1994 29-10-1996 14-10-1997
DE 19525607 A	16-01-1997	AU 722943 B AU 6656796 A BG 102200 A BR 9609796 A CA 2226718 A CN 1190904 A CZ 9800118 A WO 9703718 A EP 0840634 A HU 9802773 A JP 11509123 T NO 980147 A PL 324530 A SK 4998 A US 6132755 A	17-08-2000 18-02-1997 31-08-1998 16-03-1999 06-02-1997 19-08-1998 17-06-1998 06-02-1997 13-05-1998 28-06-1999 17-08-1999 13-03-1998 08-06-1998 09-09-1998 17-10-2000
WO 9828037 A	02-07-1998	AU 722574 B AU 5529498 A CN 1233967 A EP 0957972 A	10-08-2000 17-07-1998 03-11-1999 24-11-1999
WO 9800193 A	08-01-1998	AU 3880697 A CA 2259437 A EP 0921840 A JP 2000513971 T	21-01-1998 08-01-1998 16-06-1999 24-10-2000
WO 9964580 A	16-12-1999	AU 4561699 A	30-12-1999
US 5865786 A	02-02-1999	US 5591123 A US 5135479 A US 4640689 A US 4622031 A US 4557723 A US 5746711 A US 5224928 A US 5605536 A US 5651768 A US 5931804 A US 4808152 A US 5653682 A US 5167617 A US 5976101 A US 4731926 A US 5358483 A AT 92775 T AT 168570 T AU 580585 B AU 3935285 A	07-01-1997 04-08-1992 03-02-1987 11-11-1986 10-12-1985 05-05-1998 06-07-1993 25-02-1997 29-07-1997 03-08-1999 28-02-1989 05-08-1997 01-12-1992 02-11-1999 22-03-1988 25-10-1994 15-08-1993 15-08-1998 19-01-1989 02-05-1986

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/15312

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5865786 A		BR 8504939 A	22-07-1986
		CA 1226777 A	15-09-1987
		DE 3587518 A	16-09-1993
		DE 3587518 D	16-09-1993
		DE 3587518 T	02-12-1993
		DE 3588190 D	27-08-1998
		DE 3588190 T	04-02-1999
		EP 0178601 A	23-04-1986
		EP 0197937 A	22-10-1986
		EP 0513879 A	19-11-1992
		IT 1186798 B	16-12-1987
		JP 1828721 C	15-03-1994
		JP 61100264 A	19-05-1986
		KR 9400071 B	05-01-1994
		MX 161423 A	24-09-1990
		WO 8602277 A	24-04-1986
		US 4856188 A	15-08-1989
		US 4713050 A	15-12-1987
		AT 45290 T	15-08-1989
		AU 563137 B	25-06-1987
		AU 3185084 A	21-02-1985
		BR 8404119 A	16-07-1985
		CA 1224993 A	04-08-1987
		DE 3479294 D	14-09-1989
		EP 0147524 A	10-07-1985
		JP 1764538 C	28-05-1993
		JP 4056627 B	09-09-1992
		JP 60060860 A	08-04-1985
		KR 9305050 B	15-06-1993
		MX 158181 A	13-01-1989
WO 9800194 A	08-01-1998	EP 0925088 A	30-06-1999